Cancer Researcher's Odyssey Benefits Many Patients

The following is a profile of Canadian researcher Alejandro R. Jadad.

An impromptu lecture to a group of young school children changed the life of Alejandro (Alex) R. Jadad, M.D., D.Phil., when he was a medical student. The children wanted to hear about drugs, but Jadad, training in one of Colombia's best medical schools, realized he knew virtually nothing about drug abuse issues "in a country that was the world leader in drug smuggling."

Shocked at his inadequacy — "It took me 5 minutes to tell them all I knew" — Jadad set out to remedy the lack of available knowledge on cocaine and other narcotics by going to the botanical gardens to study the chemistry of plants. He even spent a weekend in an illicit drug "factory," learning the drug dealers' jargon, taking samples for later study, and interviewing drug users.

From that intensive, hands-on odyssey, he designed treatments for crack overdoses and — at age 19 — became Colombia's medical expert on cocaine, representing his country at international meetings and regularly promoting drug prevention on national television. This set him on a course that would lead him away from Colombia in search of ways to improve medical care through quality research.

In the 15 years since then, Jadad has built an international reputation as a rigorous clinical research methodologist and an advocate for patient involvement in medical research.

Today, Jadad is assistant professor in the Health Information Research Unit, Department of Clinical Epidemiology and Biostatistics and an investigator in the Supportive Cancer Care Research Unit at McMaster University in Hamilton, Ontario, Canada. And at age 34, he has already challenged a popular method for treating cancer pain, plus a few other common practices in pain relief; developed the first validated tool for assessing the quality of randomized trials as cited in the journal *Controlled Clinical Trials,* in 1996; and earned the friendship and admiration of patients and colleagues by advocating greater consumer involvement in medical decision making.

Daniel B. Carr, M.D., calls Jadad's work "profoundly important." Carr is vice chair for research in the Department of Anesthesia at New England Medical Center in Boston. He was co-chair of the Agency for Health Care Policy and Research's panel that developed guidelines on management of acute pain and of cancer-related pain. Jadad has "begun the large and long-term task of placing pain management on an evidence-based foundation. Plus he's [using] consumer representation and advocacy in the formation of clinical care algorithms and clinical policies," Carr noted.

Dr. Alejandro R. Jadad

"I'm prepared to challenge the system and challenge myself continuously," said Jadad. His five areas of research are: supportive care, including pain relief and palliative care; evidence-based decision making; patient and family involvement in decisions; informatics and the challenges of information overload; and diversity in education and research. Any project he works on must address at least three of those five domains, he said.

"Alex is the kind of person who promises a lot and always delivers more," said George P. Browman, M.D., M.Sc., a medical oncologist and former chair of McMaster's Department of Clinical Epidemiology and Biostatistics, who was Jadad's supervisor until moving to a new position as director of the Evidence-Based Cancer Care Program for Cancer Care Ontario, the governmental agency that oversees cancer care throughout that province.

The Evidence-Based Movement

Soon after completing a residency in anesthesiology in Colombia, Jadad landed a fellowship at Oxford University in England, a leading center for narcotics and pain relief research.

Moving from Colombia, where — he said — question-asking was strongly discouraged, to Oxford, where he was paid to ask questions and search for answers, was a dream come true. "It was like a candy store for me," he recounted.

Iain Chalmers, M.B., director of the U.K. Cochrane Center in Oxford, encouraged Jadad to pursue a doctorate on the methodology of systematic reviews, something never before done by a medical doctor. The Cochrane Center had just opened to facilitate systematic reviews of research evidence across all areas of healthcare. With the guidance

of Chalmers and Henry J. McQuay, D.M., Oxford's expert in pain relief research, Jadad focused his doctoral thesis on a meta-analysis of research on pain management.

Along with creation of the largest database of randomized trials on pain control, Jadad developed new methods to combine evidence in pain relief and other areas, identified multiple gaps in pain relief research, and designed the first validated tool for evaluating randomized clinical trials. He also debunked the theory that opiates were incapable of relieving neuropathic pain, which is experienced by 30% to 40% of cancer patients when tumors invade nerves or therapy damages them.

What followed was a postdoctoral fellowship at McMaster University in Hamilton, Ontario, a leading institution in the study of health research methodology and supportive care issues where interest in consumer participation was growing. McMaster is also the place where the term "evidence-based medicine," or EBM, was coined in the early 1990s.

In evidence-based medicine, medical decisionmaking is based on the best available data — an attempt to bridge the gap between the research findings of randomized trials and actual patient care.

Skewering Unsupported Dogma

At McMaster, Jadad and Browman used EBM methods to scrutinize the World Health Organization's cancer pain guidelines and analgesic ladder, which had introduced the oft-repeated claim that up to 90% of cancer pain is treatable. Their systematic review showed that not a single controlled study had assessed the proportion of patients able to receive adequate pain relief following use of the ladder.

Browman recalled the reaction to their 1995 article in the *Journal of the American Medical Association* (*JAMA*) on the WHO ladder, "The response we got was hostile." People saw the WHO ladder as a very useful policy tool and a way to highlight the importance of pain management.

"We agreed with that. But we said the tool had not been validated by the kind of evidence that's usually demanded. We didn't say throw it away; we said that calling the ladder a validated instrument was stifling new efforts to validate it." Jadad and Browman were concerned about setting pain treatment goals to judge health professionals' performance based on an untested instrument. Since that initial response, new attempts to evaluate and improve the ladder have begun.

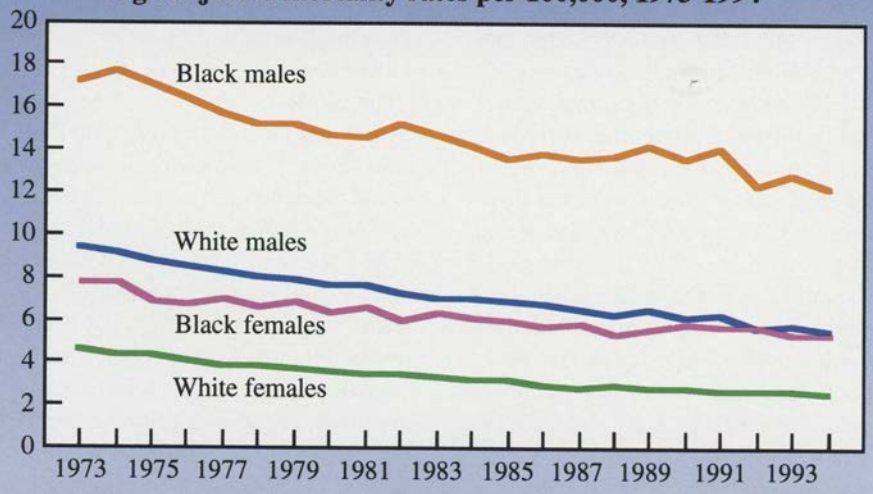
"Alex has only been on the faculty for 2 years, and he is already seen as among the world's leaders in systematic

Stat Bite

Stomach Cancer Mortality Trends in U.S. Men and Women

U.S. death rates for stomach cancer are among the lowest in the world and have been dropping since the 1930s. The advent of widespread refrigeration, which reduced food contaminants and permitted greater availability of fresh fruits and vegetables year round, is commonly cited as one cause for the drop. Since the National Cancer Institute began collecting data in 1973, the overall mortality rate for stomach cancer has declined 38%.

Age-adjusted mortality rates per 100,000, 1973-1994



Sources: *SEER Cancer Statistics Review, 1973-1994; Cancer Rates and Risks*, 4th edition.
Note: Rates are age adjusted to the 1970 U.S. standard population.

reviews," Browman noted. Jadad is director of the Evidence-Based Practice Center at McMaster, funded by the U.S. Agency for Health Care Policy and Research, and the only non-U.S. center. He is also co-director of the Canadian Cochrane Center and one of four editors of the Consumers and Communication Cochrane Review Group, which is producing systematic reviews of the best available evidence on how to communicate with patients and other health care consumers.

Patient Empowerment

In Colombia, Jadad had noticed how little decision-making power patients had and how poorly their pain was managed. Similarly, in England, many patients were passive and very tolerant of whatever interventions they received. Then in Canada, separate illnesses in his two young daughters showed him how little he, as a physician, had to say on their care. He observed the same shortcomings in research.

"We were measuring outcomes of interest to researchers and funders — talking to researchers, not patients," Jadad recalled. His doctoral review of 8,000 randomized trials on pain revealed that the wrong questions were often being asked. Outcomes were always selected by the researchers to answer academic questions rather than clinically relevant questions. Jadad and Lisa Bero, Ph.D., of the University of California at San Francisco, labeled the situation "knowledge for understanding rather than knowledge for action" in a 1997 article in *Annals of Internal Medicine*.

As a result of what he saw as a flawed research focus, "every time I tried to give meaningful advice to a patient, I was falling short," Jadad admitted. "Patients started telling me: 'Alex, show us that it's possible to do better. We are not satisfied.'"

So at Oxford he began teaming up with patients to do research. First, they helped him search the literature for randomized trials on pain control, helping him assemble the database of pain studies. Later, at McMaster, in response to a challenge from patients there, Jadad and colleagues identified more than 220 methods for measuring pain. In not one case had patients been asked the clinical value of the measurements.

Then, together with a team of patients, family members, and health professionals, he set about to develop a new pain management guide. The team described the main characteristics of an effective guide and studied research evidence on pain management, communication, and guideline development. Irene Pirocchi, a patient diagnosed with multiple myeloma 14 years ago who experiences severe bone pain, was a member of the development team. "I think that most patients just simply never consider working with their doctor," she said. Pirocchi calls Jadad's approach — working with patients and their families to understand the disease so that they can join in decision making, "marvelous."

In a pilot test with more than 200 consumers, physicians, and nurses, the guide received high marks. The team is awaiting funding to do a randomized trial. They hope to be able to demonstrate that the guide can be administered in a waiting room, without the costly coaching required for many other instruments.

With the same patient-participation approach, Jadad is developing the methodology to create consumer versions of clinical practice guidelines and more patient-centered outcomes measures. "If you're building a car, you make sure to sit people on the cushion. In health care, we don't do this frequently enough," he declared.

Internet Explosion

Recognizing that patients and other consumers need scientific information presented in a creative way, Jadad sees great potential — and danger — in the Internet. Patients are already bringing to their doctors information from the Internet. "The problem is that now they can't tell high-quality information from poor," Jadad said. This month, *JAMA* will publish his critique of instruments that evaluate health information for the Internet, which are often used to market Web sites.

In addition, Canada's National Health Research and Development Program is funding a 2-year survey by Jadad of 18,000 patients and family members to determine the characteristics of people who use the Internet for medical information and those who don't, how useful the Internet is to these users, and how consumers judge the information they find.

Jadad's inquisitiveness and eye-opening family experiences with the healthcare system coupled with his training in evidence-based methodologies give him a unique perspective to advance research on empowering patients, according to Browman. "It's like approaching something you strongly believe in in a way that your beliefs don't interfere with your judgment," Browman said.

Jadad will be at this for a while. In September 1997, he received a National Health Research Scholar Award, which funds 75% of his salary for the next 5 years to study and enhance consumer access to and use of best available evidence. He's got big plans for those 5 years.

—*Cori Vanchieri*